

contraindication (possible tumor spread), the final role of hysteroscopy is uncertain. At present few data are available to strongly suggest an important role for hysteroscopy in patients with repeated abortions, congenital anomalies and unexplained infertility.

Contraindications are active uterine bleeding, recent uterine perforation or infection, and pregnancy. Complications (which occurred only rarely among 600 patients) include bleeding, infection, uterine perforation, and reaction to either the anesthetic or the medium used.

In summary, hysteroscopy is an extremely valuable technique for gynecologists. Although the indications are few, this technique greatly enhances our ability to care for patients with the conditions discussed. It is likely that future advances in hysteroscopy will lead to its even wider application.

CHARLES M. MARCH, MD

REFERENCES

- March CM, Israel R: Intrauterine adhesions secondary to elective abortion: Hysteroscopic diagnosis and management. *Obstet Gynecol* 48:422-424, Oct 1976
 March CM, Israel R, March AD: Hysteroscopic management of intrauterine adhesions. *Am J Obstet Gynecol* 130:653-657, Mar 15 1978

The Role of Bromocriptine in Gynecologic Practice

THREE RECENTLY DEVELOPED diagnostic techniques, a radioimmunoassay for prolactin (PRL), hypocycloidal polytomography of the sella turcica and computerized axial tomography (CAT scans), together with the release of the ergot alkaloid 2-Br- α -ergocryptine have signaled the arrival of a new era in medicine. We are now able to *diagnose* and to *treat* ailments which were barely understood at the beginning of the last decade.

It appears that the prevalence of galactorrhea, of pituitary adenomas and of menstrual abnormalities has increased. However, since more sensitive diagnostic techniques are available, we may be searching for these problems more carefully and the increased incidence may only be apparent. Many patients who have galactorrhea and most of those who have pituitary adenoma have hyperprolactinemia.

The use of bromocriptine has been approved only for women who have amenorrhea, galactorrhea and hyperprolactinemia but in whom there is no evidence of a pituitary tumor. A careful investigation is mandatory to select candidates for treatment. Galactorrhea is any unilateral or bilateral breast discharge which is neither purulent nor hemorrhagic in a patient who has not breast-fed nor been pregnant within the preced-

ing 12 months. The presence of fat globules in the secretions confirms the milky nature of the discharge.

All patients with inappropriate lactation should have a serum thyroid stimulating hormone (TSH) determination in addition to a measurement of the PRL concentration. Primary hypothyroidism has been associated with amenorrhea, galactorrhea and hyperprolactinemia. If the TSH level is elevated, thyroid replacement therapy should be instituted. Radiographs of the sella turcica should also be obtained—initially cone views, but if these show no abnormalities, polytomography should be carried out. CAT scans are indicated in women with hyperprolactinemia to rule out a suprasellar mass which may be present even if the sellar architecture remains intact.

Women with hyperprolactinemia usually have oligomenorrhea or amenorrhea because of reduced pituitary FSH and luteinizing hormone production. This reduction then leads to anovulation and menstrual abnormalities. Bromocriptine reverses this defect by a dual action. This dopamine receptor agonist stimulates the release of prolactin-inhibiting factor via hypothalamic centers and also directly inhibits the release of prolactin by the pituitary gland. Serum PRL levels return to normal and thus the inhibition of cyclic pituitary and ovarian function is removed.

Treatment should be started with one 2.5 mg tablet per day to be taken with a meal (to reduce the chance and the severity of nausea). Within four to seven days the dose is doubled and this increase maintained. After four weeks the patient should be reexamined and another serum prolactin level obtained. If the serum PRL level or the amount of galactorrhea (or both) is unchanged, a third tablet should be added. This is the maximum dose. Approximately 80 percent of patients who are treated with bromocriptine respond with a return of serum PRL levels to normal (usually within one to two weeks), the resumption of ovulatory menstrual cycles (usually in four to six weeks) and the cessation of lactation (eight to ten weeks).

Although more than 800 pregnancies secondary to bromocriptine treatment have been reported with no increase in the frequency of congenital anomalies or multiple gestations, this agent may not yet be used for the management of infertility. (It should be remembered that data on more than 2,000 pregnancies had been reviewed before the release of clomiphene.) Therefore, a mechanical

method of contraception should be utilized during treatment. Therapy should be continued until a remission has occurred for a maximum of six months. Unfortunately, after stopping therapy with bromocriptine most patients have a recurrence of symptoms.

Side effects include nausea (usually transient) and vomiting in some patients. A variety of other gastrointestinal side effects as well as headaches, dizziness, lightheadedness and nasal congestion have been reported occasionally.

In the future, bromocriptine may be used for many indications. Of paramount interest will be its use in treatment of infertility, suppression of postpartum lactation and therapy for patients who have prolactin-secreting pituitary tumors. Other uses may be amenorrhea-galactorrhea without hyperprolactinemia, luteal phase defects, acromegaly, Parkinson disease, and some cases of breast carcinoma. Early reports of its use for men with hypogonadotropic hypogonadism have also been favorable.

In summary, the availability of bromocriptine has opened new vistas. This agent appears to be highly effective in therapy for patients with a wide variety of conditions. Factors limiting its widespread application in the immediate future are the occasionally catastrophic complications of pregnancy in a patient with a pituitary tumor and a still unproved freedom from teratogenic effects.

CHARLES M. MARCH, MD

REFERENCES

Davajan V, Kletzky O, March CM, et al: The significance of galactorrhea in patients with normal menses, oligomenorrhea, and secondary amenorrhea. *Am J Obstet Gynecol* 130:894-904, Apr 15, 1978

March CM, Kletzky OA, Davajan V: Clinical response to CB-154 and the pituitary response to thyrotropin-releasing hormone-gonadotropin-releasing hormone in patients with galactorrhea-amenorrhea. *Fertil Steril* 28:521-525, May 1977

The Pap Test: How Often?

CARCINOMA OF THE CERVIX ranks as the second most common gynecologic malignant condition with 20,000 new cases and 7,400 deaths reported in 1978. A preponderance of evidence indicates a continuum from dysplasia through carcinoma in situ (CIS) to invasive cancer. Although some precursor lesions may remain stable for years, or even regress, most are thought to progress over a variable period of time. On this basis it is logical to diagnose the dysplasias and CIS as early as possible because the therapy of cervical intraepithelial neoplasia (CIN) is relatively simple and complication-free compared with the therapy of invasive cervical carcinoma, and can allow pres-

ervation of reproductive function. These considerations are of even greater importance as the incidence of CIN lesions has reached epidemic proportions in the younger, sexually-active population. It has been estimated that more than 40,000 cases of cervical carcinoma in situ were detected in 1976; the annual rate appears to have increased since that report.

Although the cytologic smear represents a proven technique for the detection of precursor cervical lesions, recent information, such as in the Walton Report, has suggested that a yearly Papanicolaou (Pap) test is not cost-effective and is unnecessary for most women. However, this contention should not be accepted without qualification. A more logical approach would be to take into consideration the relative risk for a given patient population. A low-risk group would include women with a history of three serially normal annual Pap tests and an historical sexual pattern which includes an active coital life commencing after age 18, and involving few sexual partners. The conditions of these persons may safely be followed by cytologic sampling every two to three years. However, a high-risk group may be identified by the following: (1) a history of first coitus or pregnancy at an early age (<18 years) and (2) multiple sexual partners or prior diagnosis by an abnormal Pap test result. Additional high-risk factors include a history of herpes virus infection and sexual partners (1) previously married to a woman with cervical carcinoma or (2) with a history of penile or prostatic carcinoma. Women in this category should undergo cytologic cervical evaluation once a year or every six months.

The case for yearly Pap tests is emphasized by a report from Fox. In a group of 547 women with abnormal Pap test results, 195 (35 percent) had a history of previous negative cytology, and 41 (7.5 percent) had three prior negative smears. In 141 women (26 percent) cytologic atypia developed in less than two years from the last normal smear. Of great significance is that in 51 of 140 women (36 percent) significant atypia developed within six months of a negative smear.

In addition, a Pap test is the single most powerful stimulus that brings women to physicians' offices for annual examinations. Carcinoma of the breast represents the greatest cause of death from cancer in women, colorectal carcinoma is third and ovarian cancer is the most frequent cause of death from gynecologic malignancy. The